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CLINICAL RESEARCH

Incidence, Temporal Trends, and Prognostic Impact of Heart Failure Complicating Acute Myocardial Infarction

The SWEDEHEART Registry (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies): A Study of 199,851 Patients Admitted With Index Acute Myocardial Infarctions, 1996 to 2008

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ABSTRACT

OBJECTIVES The aim of this study was to examine temporal trends in the incidence and outcomes of heart failure (HF) complicating acute myocardial infarction (AMI) in a large national cohort.

BACKGROUND There are limited and conflicting data concerning temporal trends in the incidence and prognostic implication of in-hospital HF that complicates AMI.

METHODS The nationwide coronary care unit registry SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) records baseline characteristics, treatments, and outcome of consecutive patients with AMIs admitted to all hospitals in Sweden. The diagnosis of HF requires the presence of crackles (Killip class ≥II) or the use of intravenous diuretic agents or intravenous inotropes. This study included 199,851 patients admitted for index AMIs between 1996 and 2008.

RESULTS The incidence of HF declined from 46% to 28% ($p < 0.001$). This decrease was more pronounced in patients with ST-segment elevation myocardial infarctions and left bundle branch block (from 50% to 28%) compared with those with non-ST-segment elevation myocardial infarctions (from 42% to 28%) ($p < 0.001$). The in-hospital, 30-day, and 1-year mortality rates for patients who developed HF during the index myocardial infarction decreased over the years from 19% to 13%, from 23% to 17%, and from 36% to 31%, respectively ($p < 0.001$ for all). Thirteen-year survival analysis showed higher mortality in patients with HF compared with those without HF (adjusted hazard ratio: 2.1; 95% confidence interval: 2.06 to 2.13).

CONCLUSIONS A marked decrease was found in the incidence of HF complicating AMI between 1996 and 2008. However, HF continues to worsen the early-, intermediate-, and long-term adverse prognostic risk after AMI.
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Heart failure (HF) is a major health problem worldwide (1,2). It carries a poor prognosis (5-year cumulative mortality of 40% to 50%) (1) and requires frequent readmissions to the hospital (35% to 50% within 6 months). Coronary heart disease and hypertension constitute the major underlying causes of HF. Both pre-existing chronic HF and the development of de novo HF as a complication of acute myocardial infarction (AMI) are associated with worsened short- and long-term outcome (3–5). The prognosis of patients after AMI has markedly improved during the past 15 to 20 years, and mortality rates from coronary heart disease in general have declined for the past 25 years in most Western countries. Remarkable changes have taken place in the factors that contribute to the incidence of post-AMI HF over the past 2 decades. Changes

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in baseline population characteristics as well as a decrease in infarct size due to salvage of myocardium by better treatment may have improved myocardial function and thus reduced the prevalence of HF after AMI (6–8). Better management of patients who develop HF may also result in improved outcomes. Previous studies have shown conflicting evidence about the incidence, temporal trends, and even prognostic impact of HF that complicates AMI (1,2,9–13). Different definitions of HF, merging of early- and late-onset HF after AMI, and different populations and study designs are reasons that could be cited for difficulties drawing clear inferences about changes in the incidence and temporal trends of post-myocardial infarction HF over the years.

By studying an unselected large cohort of patients with index AMIs registered prospectively in the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies)/RIKS-HIA (Register of Information and Knowledge About Swedish Heart Intensive Care Admissions) registry, the aim of this study was to describe the incidence, temporal trends, and prognostic significance of in-hospital post-AMI HF over a time period of 13 years.

METHODS

THE SWEDEHEART/RIKS-HIA REGISTRY. The RIKS-HIA database was established as a national quality registry in 1995 and today includes all Swedish hospitals that provide acute coronary care (n = 72). The registry enrolls consecutive patients admitted to coronary care units because of symptoms suggestive of acute coronary syndromes. Information is collected prospectively for more than 100 variables, including baseline characteristics, electrocardiographic findings, examinations, interventions, in-hospital complications, discharge medications, and diagnoses. The whole process has been described elsewhere (14,15). The variables in RIKS-HIA comply with the international Cardiology Audit and Registration Data Standards (16). This study included all patients in the registry with index diagnoses of AMI who were admitted between 1996 and 2008. If a patient was registered several times, only the first index event was included in the analysis.

From 1996 to 2001, the criteria for the diagnosis of AMI were based on the World Health Organization criteria from 1994 (17,18), combining symptoms, electrocardiographic changes, or both with an increase in a biochemical marker (mainly creatine kinase-MB) exceeding twice the upper reference level as the biochemical criterion (17,18). The electrocardiogram was evaluated for the presence or development of Q waves, ST-segment changes, T-wave inversions, or bundle branch block. From late 2001, the criteria for the diagnosis of AMI according to the European Society of Cardiology, American College of Cardiology, and American Heart Association consensus document, using troponin T or I or eventually creatine kinase-MB level exceeding the 99th percentile in a healthy population together with either typical symptoms or electrocardiographic changes, were adopted.

Mortality data were obtained by merging the RIKS-HIA database with the Swedish population register, which includes information on the vital status of all Swedish citizens through December 31, 2008. Histories of HF, stroke, renal failure, chronic pulmonary disease, dementia, cancer, AMI, and peripheral

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction
CI = confidence interval
EF = ejection fraction
HF = heart failure
IV = intravenous
LBBB = left bundle branch block
NSTEMI = non-ST-segment elevation myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction

the sponsors participated in the design or conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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TABLE 1 Baseline Characteristics

Variable	n*	1996-1997 (n = 17,105)	1998-1999 (n = 27,503)	2000-2001 (n = 30,600)	2002-2003 (n = 32,244)	2004-2005 (n = 31,645)	2006-2007 (n = 31,873)	2008 (n = 15,625)
Age (yrs)	199,723	70.2 ± 11.7	70.7 ± 11.9	71.2 ± 12.0	71.4 ± 12.1	71.3 ± 12.2	70.9 ± 12.3	70.9 ± 12.5
Women	199,851	5,992 (35.0%)	9,909 (36.0%)	11,271 (36.8%)	12,122 (37.6%)	11,718 (37.0%)	11,726 (36.8%)	5,797 (37.1%)
Diabetes	199,851	3,535 (21.1%)	5,860 (21.9%)	6,733 (22.5%)	7,149 (22.6%)	7,040 (22.4%)	7,157 (22.5%)	3,471 (22.3%)
Hypertension	194,090	5,382 (32.5%)	8,709 (32.9%)	10,383 (35.1%)	11,889 (38.1%)	12,615 (40.9%)	14,152 (45.0%)	7,256 (47%)
Current smokers	181,117	3,413 (21.7%)	5,595 (22.3%)	6,168 (22.4%)	6,663 (22.6%)	6,707 (23.9%)	6,831 (23.5%)	3,267 (23.0%)
Medical history								
MI	199,851	2,737 (18.4)	4,040 (16.9)	4,169 (15.5)	4,071 (14.4)	3,628 (12.7)	3,115 (10.7)	1,436 (10.6)
CHF	199,851	2,005 (11.7%)	3,347 (12.2%)	3,797 (12.4%)	3,974 (12.3%)	3,476 (11.0%)	3,274 (10.3%)	1,519 (9.7%)
Stroke	199,851	1,785 (10.4%)	2,991 (10.9%)	3,446 (11.3%)	3,722 (11.5%)	3,459 (10.9%)	3,354 (10.5%)	1,533 (9.8%)
COPD	199,851	1,036 (6.1%)	1,901 (6.9%)	2,285 (7.5%)	2,696 (8.4%)	2,689 (8.5%)	2,896 (9.1%)	1,504 (9.6%)
PAD	199,851	969 (5.7%)	1,516 (5.5%)	1,751 (5.7%)	1,865 (5.8%)	1,777 (5.6%)	1,696 (5.3%)	814 (5.2%)
Renal failure	199,851	245 (1.4%)	432 (1.6%)	574 (1.9%)	714 (2.2%)	745 (2.4%)	814 (2.6%)	444 (2.8%)
Previous invasive treatment								
PCI	194,858	495 (3.0%)	858 (3.2%)	1,092 (3.7%)	1,324 (4.2%)	1,451 (4.6%)	1,780 (5.6%)	911 (5.9%)
Previous CABG	195,083	673 (4.7%)	1,169 (4.4%)	1,584 (5.4%)	1,825 (5.8%)	1,995 (6.4%)	2,012 (6.3%)	994 (6.4%)
Revascularization therapy (PCI)								
NSTEMI	187,077	2,482 (27%)	4,411 (28.6%)	5,771 (32.2%)	7,138 (35.4%)	8,638 (43.2%)	9,938 (47.5%)	5,488 (50.8%)
STEMI/LBBB	187,077	2,355 (32.5%)	3,962 (35.8%)	4,809 (41.8%)	5,526 (50.8%)	6,912 (64.2%)	7,624 (73.7%)	3,640 (80.6%)
Reperfusion therapy STEMI/LBBB								
Thrombolysis	197,542	4,543 (94%)	6,771 (91.1%)	6,702 (87.3%)	5,162 (72.2%)	2,662 (37.1%)	940 (12.6%)	299 (8,5%)
Primary PCI	197,542	290 (6%)	663 (8.9%)	974 (12.7%)	1,984 (27.8%)	4,505 (62.9%)	6,492 (87.4%)	3,232 (91,5%)
Thrombolysis or PCI		62.8%	63.1%	61.4%	61.1%	63.3%	71%	77.1%
Medications at entry and discharge								
Aspirin								
Admission	190,131	5,808 (34.5%)	9,900 (36.9%)	11,333 (37.8%)	12,046 (38.2%)	11,500 (36.7%)	11,408 (36.1%)	5,407 (34.9%)
Discharge	190,131	12,279 (81.7%)	20,778 (81.9%)	23,727 (81.8%)	25,463 (82.4%)	26,911 (86.2%)	28,266 (89.0%)	14,077 (90.3%)
Beta-blockers								
Admission	195,734	5,146 (30.6%)	8,716 (32.5%)	10,407 (34.7%)	11,466 (36.5%)	11,398 (36.4%)	11,249 (35.6%)	5,430 (35.1%
Discharge	189,830	11,243 (75.0%)	19,330 (76.3%)	23,267 (80.3%)	25,432 (82.5%)	26,209 (84.0%)	27,191 (85.6%)	13,473 (86.5%)
Calcium-channel blockers								
Admission	195,422	3,020 (17.9%)	4,516 (16.9%)	4,848 (16.2%)	4,962 (15.9%)	4,889 (16.2%)	5,050 (16.0%)	2,652 (17.1%)
Discharge	188,594	2,070 (13.9%)	3,503 (14.0%)	3,698 (12.9%)	3,926 (12.9%)	3,720 (12.0%)	4,292 (13.5%)	2,244 (14.4%)
ACE inhibitors/ARBs								
Admission	195,721	2,383 (14.2%)	4,055 (15.1%)	5,241 (17.5%)	6,554 (20.8%)	7,401 (23.6%)	8,681 (27.4%)	4,630 (29.9%)
Discharge	189,259	5,519 (36.9%)	9,250 (36.8%)	12,305 (42.8%)	14,509 (47.2%)	17,257 (55.3%)	20,006 (63.0%)	10,609 (68.1%)
Statins								
Admission	195,549	1,015 (6.0%)	2,317 (8.7%)	3,870 (12.9%)	5,183 (16.5%)	5,774 (18.4%)	6,861 (21.7%)	3,655 (23.6%)
Discharge	188,976	3,199 (21.5%)	8,511 (33.9%)	13,721 (47.7%)	17,963 (58.5%)	21,294 (68.3%)	24,390 (76.8%)	12,564 (80.6%)
Clopidogrel								
Admission	195,549	0	101 (0.4%)	353 (1.2%)	1,095 (3.5%)	1,560 (5.0%)	1,368 (4.3%)	627 (4.0%)
Discharge	188,976	0	1,108 (4.4%)	3,948 (13.6%)	11,439 (37.0%)	17,564 (56.3%)	21,662 (68.2%)	11,424 (73.3%)

Continued on the next page

vascular disease were obtained by merging with the National Patient Register, which includes diagnoses for all patients hospitalized in Sweden from 1987 onward.

To ensure the validity of the information entered into the database, 1 specially trained monitor visited participating hospitals and compared information in the patient records, including electrocardiograms, with the information entered into the RIKS-HIA database involving 30 to 40 randomly chosen patients from each hospital. Data quality were monitored in 5,446 random records from all participating hospitals, comprising 299,530 measurements, demonstrating 95% overall agreement between the registered information and patient records. All patients for whom data were entered into the RIKS-HIA database were informed about their participation in the registry (patients could request to be excluded) and the long-term follow-up. The merging with other registries was approved by the National Board of Health and Welfare. Ethical approval of the study was obtained from the Ethics Committee of Uppsala University.

TABLE 1 Continued

Variable	n*	1996–1997 (n = 17,105)	1998–1999 (n = 27,503)	2000–2001 (n = 30,600)	2002–2003 (n = 32,244)	2004–2005 (n = 31,645)	2006–2007 (n = 31,873)	2008 (n = 15,625)
Other in-hospital treatments								
UFH	118,396	3,466 (20.8%)	4,761 (17.8%)	4,494 (15.2%)	2,987 (9.5%)	2,476 (7.9%)	2,068 (6.5%)	981 (6.3%)
LMWH and fondaparinux (after 2006)	118,181	2,610 (15.6%)	7,990 (29.9%)	12,455 (42.0%)	17,730 (56.7%)	20,710 (66.1%)	21,609 (68.1%)	10,413 (66.9%)
Glycoprotein IIb/IIIa inhibitors	85,402	–	1,221 (6.2%)	2,232 (7.9%)	3,611 (11.8%)	7,708 (25.6%)	8,781 (27.6%)	3,960 (23.4%)
Inotropes	194,802	1,241 (7.5%)	1,591 (6.0%)	1,521 (5.2%)	1,327 (4.3%)	1,317 (4.2%)	1,171 (3.7%)	537 (3.4%)
CPAP	187,553	1,013 (6.2%)	1,593 (6.0%)	1,735 (6.0%)	1,815 (6.1%)	1,836 (5.9%)	1,711 (5.4%)	763 (4.9%)
IV diuretic agents	195,325	6,938 (41.7%)	10,027 (37.7%)	10,436 (35.4)	10,047 (32.3)	9,449 (30.2)	8,189 (25.8)	3,522 (22.6%)
Complications								
New AF	193,410	2,015 (12.1%)	2,251 (8.5%)	2,277 (7.7%)	2,228 (7.2%)	1,619 (5.3%)	1,420 (4.6%)	710 (4.7%)
CPR (VT/VF/other)	175,234	1,077 (6.4%)	1,583 (5.8%)	1,578 (5.4%)	1,481 (4.9%)	1,364 (4.3%)	1,132 (3.6%)	553 (3.5%)
AV block II or III	194,706	759 (4.6%)	921 (3.5%)	892 (3.1%)	792 (2.6%)	649 (2.1%)	577 (1.8%)	276 (1.8%)
Reinfarction	190,510	702 (4.4%)	790 (3.1%)	732 (2.5%)	643 (2.2%)	611 (2.0%)	463 (1.5%)	182 (1.2%)
Mechanical (rupture, VSD, MI)	62,455	NA	NA	NA	NA	52 (0.4%)	91 (0.3%)	37 (0.3%)
Hypotension (SBP <90 mm Hg)	75,697	3.7%	2.3%	2.6%	2.9%	2.5%	2.2%	2.2%
Cardiogenic shock	72,358	NA	NA	NA	NA	697 (2.7%)	687 (2.2%)	344 (2.2%)

Values are mean ± SD or n (%). *Number of patients with known values.

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; ARB = angiotensin II receptor blocker; AV = atrioventricular; CABG = coronary artery bypass grafting; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; CPR = cardiopulmonary resuscitation; IV = intravenous; LBBB = left bundle branch block; LMWH = low-molecular weight heparin; MI = myocardial infarction; NA = not available; NSTEMI = non-ST-segment elevation myocardial infarction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; SBP = systolic blood pressure; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin; VF = ventricular fibrillation; VSD = ventricular septal defect; VT = ventricular tachycardia.

DEFINITION OF HF. In this study, HF was defined as the presence of pulmonary rales, administration of intravenous (IV) diuretic agents, continuous positive airway pressure, or the use of IV inotropic drugs, as documented in the RIKS-HIA protocol. Evaluation of the degree of severity was assessed by using the Killip classification. Cardiogenic shock was defined as systolic blood pressure ≤90 mm Hg for >30 min, and hypovolemia was ruled out in the presence of signs of organ hypoperfusion or if the cardiac index was <1.8 l/min/m^2 or if IV inotropes or an intra-aortic balloon pump were used.

STATISTICAL ANALYSES. Data are reported as proportions, mean ± SD, and median. The incidence of clinical HF and estimated proportions of patients and their baseline characteristics, as well as mortality over time, were evaluated by comparing cohorts of patients admitted over 2-year periods. Trend tests were performed for the variables for which we reported temporal trends using chi-square tests for trend with the linear-by-linear model.

A logistic regression model was used to identify independent predictors of developing HF. Included in the analyses were baseline data before presentation and known to influence the risk for developing HF: age, sex, hypertension, diabetes, prior HF, prior myocardial infarction, prior coronary artery bypass grafting, and prior medication (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, beta-blockers, calcium antagonists, digoxin, and diuretic agents) and time period. A logistic regression model was also used to identify independent predictors of death at 1 year in patients with acute HF. The variables mentioned previously were entered into the model. To examine the independent association between acute HF and subsequent long-term mortality, a Cox regression model was used. Variables in the model were age, sex, hypertension, diabetes, prior stroke, atrial fibrillation, and time period. Long-term mortality was presented as a Kaplan-Meier plot for patients with HF and those without HF. All analyses were performed with SPSS version 19 (SPSS, Inc., Chicago, Illinois).

RESULTS

PATIENTS WITH AMI AND HOSPITALS. During the 13-year period, 199,851 patients fulfilled the criteria for AMI and were included in the study. The number of sites participating in the registry increased from 47 sites providing 17,105 patients in the first period (1996 and 1997) to a fairly stable number of 70 to 75 sites with approximately 32,000 patients in the 2-year periods from 1998 onward.

BACKGROUND FACTORS. There was a small increase in the mean age of the patients (from 70.0 to 70.9 years). The proportion of women in the study population also increased modestly (from 35.0% to 37.1%).

Diabetes mellitus was present in 21.1% of the population in 1996 and 1997 and in 22.3% in 2008. Hypertension increased markedly from 32.5% in 1996 and 1997 to 47.0% in 2008. The proportion of current smokers showed a slight increase (from 21.7% to 23.0%). The proportion of patients with history of AMI decreased from 17.8% to 10.6%. Similarly, the proportion of patients with histories of congestive HF decreased from 11.7% to 9.7% (Table 1).

HF DURING INDEX MYOCARDIAL INFARCTION. The incidence of HF during hospitalization declined from 46% in 1996 and 1997 to 28% in 2008 ($p < 0.001$, chi-square test for trend). This decrease was more pronounced in patients with ST-segment elevation myocardial infarctions (STEMIs) or left bundle branch block (LBBB) (from 50% to 28%) compared with those with non-ST-segment elevation myocardial infarctions (NSTEMIs) (from 42% to 28%) ($p < 0.001$). In patients with HF, the proportion of women increased from 39% to 46% over the years. The proportion of patients with HF with normal ejection fractions (EFs) (≥50%) increased from 18% in 1998 and 1999 to 30% in 2008, whereas the proportion with EFs <40% decreased from 48% to 44% (Table 2). In 1996 and 1997, 35% of all patients with AMIs had pulmonary rales of some grade (Killip class ≥II), whereas the corresponding figure for 2008 was 13%. The use of IV inotropic drugs, IV diuretic agents, and continuous positive airway pressure decreased progressively (Table 1). The proportion of patients with cardiogenic shock was 2.7% in 2004 and 2005 and 2.2% in 2008, but we cannot report for the first 4 period intervals because of changes in variable definition. At the beginning of the study period (1996 and 1997), 61%, 39%, and 17% of patients >75, 50 to 75, and <50 years of age, respectively, showed clinical HF during hospitalization for index AMIs, whereas the corresponding numbers for the respective ages in 2008 were 41%, 18%, and 11%. In 1996 and 1997, 72% of patients with previously known HF showed signs of decompensation during hospitalization for index AMIs, whereas 58% of patients with histories of HF showed signs of decompensation in 2008. The figures for those without previous diagnoses of HF were 34% and 26%, respectively.

Multivariate analysis showed that every additional year in age increased the risk for HF (odds ratio [OR]: 1.054; 95% confidence interval [CI]: 1.05 to 1.06) and every subsequent period of 2 calendar years decreased the risk (OR: 0.86; 95% CI: 0.85 to 0.87). Women with AMIs had an increased risk for developing HF (OR: 1.15; 95% CI: 1.12 to 1.19) across the study period. Risk factors for clinical HF during hospitalization for an index AMI included history of AMI (OR: 1.21; 95% CI: 1.16 to 1.26), diabetes mellitus (OR: 1.33; 95% CI: 1.29 to 1.37), hypertension (OR: 1.07; 95% CI: 1.05 to 1.09), and history of chronic HF (OR: 2.2; 95% CI: 2.1 to 2.3).

AMI TREATMENT. The use of percutaneous coronary intervention (PCI) showed progressive increases in patients with STEMIs and LBBB and those with NSTEMIs (Table 1). Reperfusion therapy (thrombolysis or PCI) was used in 62.8% of patients with STEMIs and LBBB in 1996 and 1997, whereas 77.1% of these patients received the treatment in 2008. In 1996 and 1997, 94% of the reperfusion therapy for patients with STEMIs and LBBB was provided as thrombolysis, whereas in 2008, 91.5% of all reperfusion treatments were provided as primary PCI. The proportion of patients who were revascularized by acute coronary artery bypass grafting was relatively unchanged (0.1% vs. 0.2%).

The use at discharge of aspirin, clopidogrel, beta-blockers, statins, and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers continuously increased over the study period, aspirin from 81.7% to 90.3%, clopidogrel from <5% to 80%, beta-blockers from 75.0% to 86.5%, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers from 36.9% to 68.1%, and statins from 21.5% to 80.6% (Table 1).

MORTALITY. The estimated in-hospital (Figure 1), 30-day, and 1-year mortality for patients with clinical HF and AMIs decreased over the years from 19%

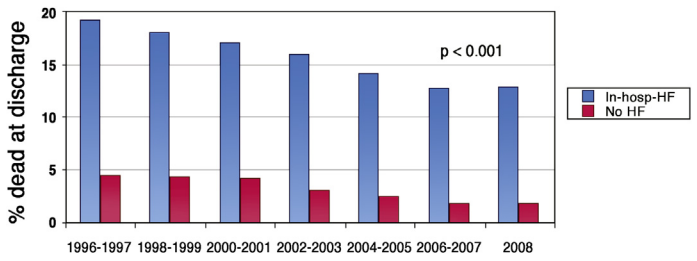
TABLE 2 Proportion of Patients With HF in Different EF Categories Over the Years

Variable	1998-1999 (n = 2,338)	2000-2001 (n = 8,148)	2002-2003 (n = 11,902)	2004-2005 (n = 16,675)	2006-2007 (n = 19,673)	2008 (n = 10,273)
EF ≥50%	175 (18%)	696 (21.4%)	1,016 (23.1%)	1,440 (25.6%)	1,662 (28.8%)	825 (30.1%)
EF 40%-49%	327 (33.6%)	1,098 (33.7%)	1,354 (30.8%)	1,468 (26.1%)	1,451 (25.1%)	696 (25.4%)
EF <40%	470 (48.4%)	1,462 (44.9%)	2,027 (46.1%)	2,726 (48.4%)	2,666 (46.1%)	1,216 (44.4%)
Total new HF/period	972 (100%)	3,256 (100%)	4,397 (100%)	5,634 (100%)	5,779 (100%)	2,737 (100%)

Values are n (%).
EF = ejection fraction; HF = heart failure.

to 13%, from 23% to 17%, and from 36% to 31%, respectively ($p < 0.001$, chi-square test for trend). The 1-year odds of death in patients with clinical HF after AMI decreased by 7% per 2 calendar years between 1996 and 2008 (OR: 0.93; 95% CI: 0.92 to 0.94), independent of age, sex, and comorbidities (**Figure 2**). The mortality increased markedly with age (OR: 1.082; 95% CI: 1.081 to 1.083). Women had 10% lower mortality than men (OR: 0.9; 95% CI: 0.8 to 0.91). Long-term survival analysis (**Figure 3**) showed higher mortality for patients with HF compared with those without HF (adjusted HR: 2.09; 95% CI: 2.06 to 2.13).

FIGURE 1 In-Hospital Mortality Rate Trends in Patients With and Without Clinical HF During Hospitalization for an Index AMI



Chi-square test for trend: $p < 0.001$. AMI = acute myocardial infarction; HF = heart failure.

DISCUSSION

Our findings indicate a steady major decrease in the incidence of HF complicating AMI regardless of sex, age, and infarct type between 1996 and 2008. Second, the relative proportion of HF with normal EF is increasing. Third, HF still carries an increased mortality risk, as observed during short-, intermediate-, and long-term follow-up. Fourth, mortality in patients who develop in-hospital HF after an index AMI is steadily decreasing with time.

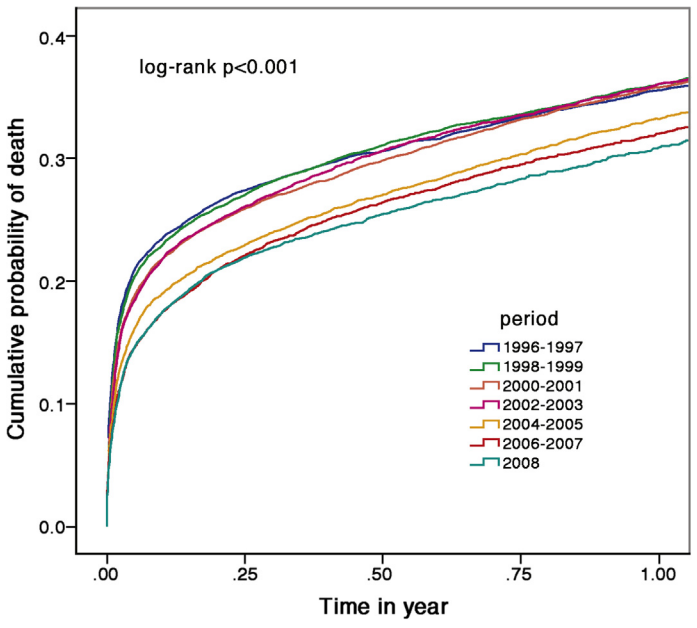
The incidence of AMI has declined in Sweden during the past few decades (5), probably due in part to reductions in smoking and levels of low-density lipoprotein cholesterol. In contrast, the diagnosis of AMI on the basis of increasingly sensitive serial biomarkers has substantially increased the detection of AMI cases, counteracting the actual declining rates of AMI. Smaller AMIs that could have been missed with previous criteria are detected with the new criteria (6,7), which in turn could contribute to a reduced risk for subsequent HF, as HF is related to infarct size (8). This in turn might partly explain the declining incidence of HF after AMI (19). However, the decline in the incidence of HF did not show an abrupt change after the institution of the new criteria. We rather saw a smooth progressive decline, suggesting other explanations, such as more frequent use of effective evidence-based treatments and changes in the burden of risk factors. The greater decrease of HF observed in patients with STEMIs compared with those with NSTEMIs also argues against the suggestion that an overall decline in HF incidence is merely a reflection of the detection of smaller infarcts.

Some previous studies have elucidated recent trends in patient characteristics, incidence of HF, treatment, and outcomes in the setting of AMI (1,2,9,10,12,13,20,21). This is the largest observational study examining temporal trends in the incidence and effect on outcomes of HF in the setting of AMI with a high national coverage of patients with AMI (22).

Our findings indicate a steady decline in the incidence of HF complicating AMI, regardless of sex and age. This is consistent with the findings of the majority of population-based studies (1,9,10,13,20,21).

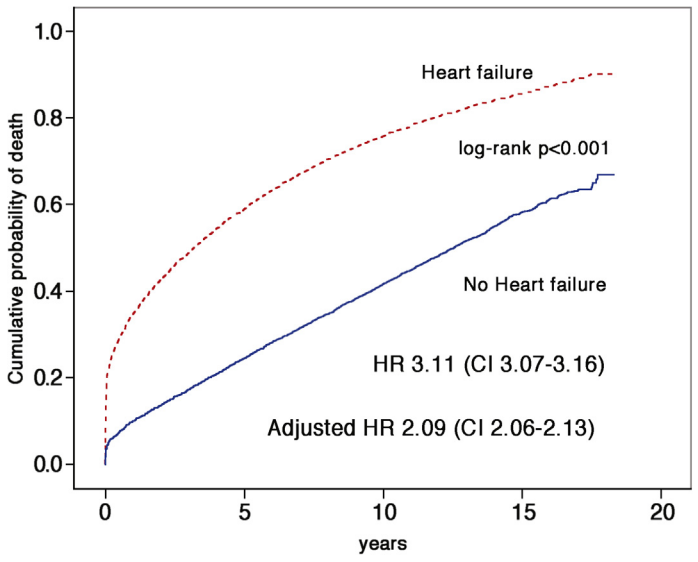
The past couple of decades have provided us with considerable improvements in the management of patients with AMIs, with increasing use of effective

FIGURE 2 1-Year Mortality for Patients With In-Hospital HF During Hospitalization for an Index AMI According to Period Intervals



Log-rank $p < 0.001$. AMI = acute myocardial infarction; HF = heart failure.

FIGURE 3 Long-Term Mortality in Patients With and Without Heart Failure



Kaplan-Meier survival estimates with adjusted hazard ratio for age, sex, period, diabetes mellitus, and hypertension; log-rank p < 0.001. CI = confidence interval; HR = hazard ratio.

evidence-based treatments. These include the more frequent use of early reperfusion in ST-segment elevation AMI that prevents myocardial cell necrosis by promptly restoring blood flow to the jeopardized myocardium and the increasing use of evidence-based pharmacological treatments that improve survival and prevent negative remodeling. The increasing use of invasive treatment strategies, particularly PCI, is likely to reduce the incidence of HF as a consequence of myocardial salvage during the initial phase of AMI (23). In our study, the decline in mortality in patients with post-AMI HF was already evident in the hospital and did not increase further during a 1-year follow-up period. The onset and progress of HF are related to both infarct size and neurohormonal activation (3). It is likely that the neurohormonal antagonists are particularly effective in the later phases after AMI rather than during hospitalization, simply because they are often not given to most patients with HF at full dose during the in-hospital phase.

It is worth noting that although men still constitute the majority of the HF group, the proportion of women progressively increased throughout the study period. We also observed an increasing proportion of HF with normal EF, which might partly reflect the increasing proportion of women with comorbidities such as hypertension.

Given the sheer size of our study population and robust data with a high degree of validity, as well as a long period of follow-up, it is likely that our findings reflect a prevailing reality. However, this contradicts the claims of a few previous studies that reported an increased incidence of post-myocardial infarction HF (2,9,12). Ezekowitz et al. (2) reported an increasing incidence of in-hospital HF after a first AMI by 25% among elderly patients from 1994 to 2000. In contrast, we saw a declining incidence across all age categories. The earlier investigators included patients managed in the primary health care system as well as in hospitals, whereas our study included only hospitalized patients with AMIs, which might have contributed to the differences in our findings.

Guidry et al. (9) and Velagaleti et al. (12) from the Framingham group observed an increase over time in the incidence of HF after AMI during early (<30-day) follow-up in their patients. The first study was based on patients with Q-wave AMIs, whereas the latter included unselected patients with AMIs. Their study populations have inherent differences compared with ours, which makes direct comparisons difficult. Furthermore, they studied limited numbers of patients. Epidemiological studies have shown that long-term mortality in patients who are diagnosed with HF has decreased markedly during the past 2 decades (23,24). The likely explanations include the rapid and effective utilization of invasive treatment strategies in patients with AMIs, better medications for HF, as well as improved secondary prevention measures of ischemic heart disease, which altogether improve the outlook for individual patients (23). Nevertheless, patients with HF after AMI deserve special attention and must still be considered a high-risk group. Their early mortality rate as well as their long-term outcomes are considerably worse than those of patients without HF, which is in accordance with earlier findings showing that left ventricular systolic function and congestive HF are important predictors of elevated mortality rates (25).

The present study had some limitations. Patients who presented with clinical HF on admission could not be distinguished from those who developed HF during hospital stay. Because of the long time period, different cardiac markers and different sampling schedules have been used, and these data can therefore not be used for comparison. We used a clinical definition of HF to identify patients with decompensated clinical HF, unlike most epidemiologic studies that use International Classification of Diseases diagnoses from patient records, which may

influence direct comparison of results. However, we have reliable and robust physiologic information on each patient compared with what can be obtained from an International Classification of Diseases–based diagnosis. In our study, as in the GRACE (Global Registry of Acute Coronary Events) study (26), HF at admission was assessed by clinical examination, which has limitations in the acute setting, as symptoms and signs may be nonspecific. Nevertheless, physical findings of pulmonary rales during hospitalization have high sensitivity, as they are signs of an unfavorable hemodynamic state and predict worse outcomes (25,27). Furthermore, our criteria for the definition of clinical HF also included the use of IV diuretic agents, IV inotropes, or continuous positive airway pressure, which increases sensitivity but may also lower specificity. Moreover, we could not report on the pattern of use of aldosterone antagonists, as this information is lacking in the registry. This study is mainly descriptive, without formalized control for multiple testing, which is a limitation. However, our findings are strongly statistically significant and clinically meaningful, and relevant differences are shown by viewing the numerical data.

CONCLUSIONS

Our findings emphasize that the incidence of in-hospital HF after AMI is steadily decreasing but remains serious when it comes to early-, intermediate-, and long-term prognosis. Patients with manifest HF after AMI have a dramatically higher risk for death compared with other patients with AMI. However, mortality is decreasing over time, showing the potential for a further decrease with even better treatment strategies.

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